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Mao, Youxin; Flueraru, Costel; Chang, Shoude; Popescu, Dan P.; Sowa, Michael G.

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Imaging of Biomedical Turbid Tissue Using Catheter Swept-Source Optical Coherence Tomography

Youxin Mao*, Costel Flueraru, Shoude Chang
Institute for Microstructural Sciences,
National Research Council Canada,
1200 Montreal Rd, Ottawa K1A 0R6 ON, Canada
[*Linda.mao@nrc-cnrc.gc.ca](mailto:Linda.mao@nrc-cnrc.gc.ca)

Dan P. Popescu, Michael G. Sowa
Institute for Biodiagnostics,
National Research Council Canada,
435 Ellice Avenue, Winnipeg, MB, Canada, R3B

Abstract—We present an optical fiber catheter-based complex swept-source optical coherence tomography (OCT) system for imaging of biomedical turbid tissue. A quadrature Mach-Zehnder interferometer based on multi-port fiber couplers was employed in our complex swept-source OCT system. A variety of fiber probes were developed for the different types of biomedical application. We demonstrate OCT images of human skin and deeper tissues by using the fiber probes and our OCT engine. The results show that catheter-based swept source OCT is an effective imaging modality for real-time diagnosis and *in vivo* applications on human turbid tissue.

Keywords—biomedical imaging; turbid tissue; optical coherence tomography; quadrature interferometer; optical fiber probe.

I. INTRODUCTION

Optical coherence tomography (OCT) [1] can image tissue structure at micrometer-scale resolution, which is becoming an increasingly important imaging tool for many biomedical applications, such as diagnosis and guided surgery. OCT relies on the interferometric measurement of coherent backscattering variation to sense the internal interface structures of test samples like biological tissues or internal layered materials. It is analogous to ultrasound B mode imaging, except that it uses infra-red light source rather than ultrasound. OCT takes advantage of the short temporal coherence length of the broadband light source used in the system to achieve precise optical sectioning in the depth dimension. In the earlier stages of OCT imaging, axial (depth) ranging is provided by low coherence interferometry, where the optical path length difference between the interferometer sample and reference arms are scanned linearly in time [2]. This method of OCT, referred to as time-domain OCT (TD-OCT), has a relatively slow imaging speed although it has demonstrated promising results for early detection of disease. Fourier domain techniques in OCT have received much attention in recent years due to its significant sensitivity and high-speed advantages over TD-OCT [3]. Fourier domain methods include spectral-domain OCT (SD-OCT) and swept-source OCT (SS-OCT). In SD-OCT, individual spectral components of low-coherence light are detected separately by the use of a

spectrometer and a charge-coupled device (CCD) array [4]. CCD arrays, however, may introduce phase washout problems during the pixel integration time. Furthermore, detection using a spectrometer and CCD array cannot implement differential optical detection. Swept-source (SS) OCT enables significant increase in imaging speed and sensitivity [3], thus overcoming the sensitivity limitations in high-speed OCT which uses standard time-domain detection. SS-OCT is particularly important for imaging in the 1300 nm wavelength range, where low-cost detector arrays used in SD-OCT are not available. The larger penetration depth of the OCT image with the 1.3 μm wavelength light source is important for the biomedical turbid tissues, such as human skin and arterial plaque, in comparison with that at 1.0 μm or shorter light source. SS-OCT could also make possible for a quadrature interferometry based on multi-port fiber couplers, for example, 3x3 quadrature interferometer [5]. Due to its ability to have instantaneous complex signals with stable phase information, OCT with a 3x3 quadrature interferometer could suppress the complex conjugate artifact naturally, therefore to doubling the effective imaging depth [6]. The phase information detection of the complex signals, it also could provides additional information of the tissue, for example, optical index change, live motion, and internal flow, to enhance image contrast, and to perform quantitative and functional measurements [7-9]. However, the limit of imaging penetration depth is still a key issue. Optical fiber probe could overcome this penetration depth limitation [10,11].

In this paper, we demonstrate an optical catheter-based complex SS-OCT for biomedical turbid tissue imaging. Mach-Zehnder interferometer based on multi-port fiber couplers was employed in our SS-OCT system. Due to its ability to measure the phase information of back-reflected signals, OCT with a quadrature interferometer could extract additional information of the tissue. These phase measurements can be used to enhance image contrast and to perform quantitative measurements. A variety of fiber probes for the different types of application were developed, for example, as small as 1 mm diameter needle probe for deeper solid tissue imaging, and

different sizes of catheters for gastrointestinal tract and inter-vascular, like inter-arterial imaging. We demonstrate OCT images of deeper tissues, for example, arterial tissue and vulnerable plaque, by using the different home-built fiber probes and an in-house OCT engine. These images offer the possibility to investigate micro-morphology located on and under the arterial surface such as incipient plaque, fat streaks, endothelium layer injuries, lipid pools, fibrous caps and macrophage accumulation. The results demonstrate that catheter-based swept source OCT is an effective imaging modality for real-time diagnosis with high potential for *in vivo* applications.

II. METHODS

A. Complex OCT system

Figure 1 shows a schematic diagram of our fiber catheter based complex SS-OCT system. The system uses a balanced compound 3x3 and 2x2 quadrature MZI interferometer. The swept source (HSL2000-HL, Santac) used in the system had a central wavelength of 1320 nm and a full scan wavelength range of 110 nm, which was sweeping linearly with optical frequency with a linearity of 0.2%. The average output power and coherence length of the swept source was 12 dBm and 10 mm, respectively. A repetition scan rate of 20 kHz was used in our system and the related duty cycle was 68%. The output light from the swept laser source was launched into the first coupler and then divided into the sample arm with 90% power and reference arm with 10% power by two fiber circulators. The reference arm was arranged with a fiber collimator and a mirror. A variable wheel attenuator was inserted between the collimator and mirror for adjusting the optical power on reference arm to achieve the highest sensitivity. The light was illuminated to a sample through a lensed single mode fiber probe with different working distance (focus distance to lens surface in air), depth of field (twice the Rayleigh range in air), and $1/e^2$ spot diameter (transverse resolution) depending on the tested samples. A galvanometer (Blue Hill Optical technologies) scanner scanned the fiber probe light transversely on the sample up to 4 mm at 20 Hz with 900 transverse pixels. The total optical power illuminating on the sample was approximately 10 dBm. The reflected sample signal was combined with the returning light from the reference mirror through the output couplers using compound 3x3, 2x2 optical couplers and the two fiber attenuators to implement a complex dual-channel balanced detection. The two outputs were digitized using a data acquisition card (DAQ) (PCI 5122, National Instruments) with 14-bit resolution and acquired at a sampling speed of 100 MS/s. The swept source generated a start trigger signal that was used to initiate the function generator for the galvo scanner and initiate the data acquisition process for each A-scan. Because the swept source was linearly swept with wave-number k , A-scans data with resolved complex conjugate artifact were obtained by a direct inverse Fourier transformation (IFT) from DAQ sampling data without any re-sampling process.

Figure 1. Schematic diagram of our fiber catheter based complex SS-OCT system using a balanced compound 3x3 and 2x2 quadrature MZI interferometer.

B. Optical fiber probe

In an OCT system, light from the probe will be directed into a tissue. Based on interaction of light with biomedical turbid tissue, the range of penetration depth is from 0.5-3 mm at near infrared wavelengths. For example, the penetration depths are 0.7 mm and 3.0 mm in human skin and liver respectively at 1300 nm, a conventional wavelength used in OCT systems. Thus, for designing an optical probe, working distance should be in the range of 0.4 – 1.2 mm in the air that depends on the tissues to be tested. The optimal depth of field is in the range of 0.8 - 1.5 mm in the air; this keeps the spot size in the range of 26 - 35 μm at the 1300 nm wavelength because the tradeoff between the depth of field and beam spot size for a Gaussian beam. Beam quality of a fiber-optic probe is crucial for the imaging system. Ideal characteristics of a fiber-optic probe include a high Gaussian beam intensity profile, an appropriate intensity-distance shape, high flexibility, and low optical aberration and loss. To date, few papers have compared in detail the actual optical performance of a fiber-based optic probe with modeling results. Swanson *et al.* and Shishkov *et al.* proposed the fiber based optic probes design, but presented the variations of probe structure instead of the characteristics of their performance [12,13]. Reed *et al.* demonstrated the usage of such probes with emphasis on their insertion loss only [14]. Yang *et al.* [15], Jafri *et al.* [16], and Li *et al.* [17] reported OCT images without detailed characterization of the used fiber lens based probes. In this section, we discuss design methods and fabrication techniques of two types of fiber lenses, GRIN and ball lenses. We compare in detail measured performance with expected theoretical performance.

The theoretical and experimental results of working distance and spot size vs. length of GRIN fiber or diameter of the ball lens (bottom x-axis), and length of fiber spacer (top x-axis) are shown in Figure 2 (a) and (b), respectively.

Table 1. Lens structures with measured beam properties.

#	L_0 (mm)	Fiber Lens		Measured Beam Properties		
		Type	L/R (mm)	Working Distance (mm)	Depth of Field (mm)	Spot Size (μm)
1	0	50/125	0.41	0.11	0.17	13
2	0	100/140	0.52	0.28	0.50	22
3	0.36	50/125	0.12	0.50	0.60	23
4	0.48	100/140	0.17	1.00	0.95	28
5	0.70	Ball-Lens	0.15	1.00	0.50	20
6	0.62	Ball-Lens	0.15	1.20	1.10	27

(a)

(b)

Figure 2: Theoretical and experimental results of working distance (a) and spot size (b) vs. length of GRIN fiber or diameter of the ball lens (bottom x axis), and length of fiber spacer (top x axis), where, lines represent the theoretical results from ZEMAX at 1300 nm, amount them, dark dotted line represent GRIN fiber lens without a fiber spacer, dark and light solid lines represent GRIN fiber lens with a constant length of fiber spacer (0.48 mm) and a constant length of GRIN fiber (0.17 mm), respectively; dark and light dash lines represent ball fiber lens with a constant length of fiber spacer (0.62 mm) and a constant diameter of the ball (0.30 mm), respectively. The related experimental results were represented by the points.

The typical measured results of the beam properties are listed in Table 1 along with detailed descriptions of the samples. The lens numbers 1-4 are GRIN fiber lenses and 5-6 are fiber ball lenses. Measured $1/e^2$ intensity beam diameters along the axial distance, measured beam profile image, and schematic diagram of the lens structure are shown in figure 3 and 4. By compensating the working distance with the depth of field and the spot size, the optimized parameters (i.e. 0.9 – 1.2 mm working distance, 0.9 – 1.1 mm depth of field, and $<30 \mu\text{m}$ spot size) are not at the position of the largest working distance, instead, the optimized positions are around 0.17 mm length of the GRIN fiber with 0.48 mm length of fiber spacer for GRIN fiber lens and 0.3 mm diameter of ball and 0.62 mm length of fiber spacer for ball fiber lens.

To further examine the beam quality of the fiber lens system, beam profile images and normalized intensity distributions with Gaussian-fitted results at the x and y directions on the three typical planes (i.e. begin-plane, center-plane, and end-plane) were measured. From the profile images and distributions shown in figure 3 and 4, the measured beam profiles match very well with Gaussian distributions at the beginning-plane and center-plane. On the end-planes, the measured and Gaussian-fitted intensity distributions generally match very well despite slight deviations on both tail ends of the distributions leading to discrepancies between the measured and Gaussian-fitted beam diameters as was shown in Figure 3. In addition, the circular shapes in the beam profile images as shown in figure 3 and 4 indicate high x and y symmetry of the beam profiles through all range of depth of field.

Figure 3. Measured and Gaussian-fitted $1/e^2$ intensity beam diameters along the axial distance (zero is the position of the lens surface) at x (horizontal) and y (vertical) radial coordination in the distance range of depth of field of the samples 1-4, which were made from the GRIN fiber lenses. Insets: measured beam profile image of sample 4 (left top) and schematic diagram of the lens structure (bottom).

Figure 4. Scanning electron micrograph (a) and measured beam profile image (b) of the fiber ball lens.

For side-view optical fiber probes, fiber beam rotators can be attached to the tip of these fiber lenses. For the GRIN fiber probe, after characterization of the lens, another fiber spacer could be fusion-spliced to the lens tip as a beam director by polishing the end of the fiber spacer to a 45 degrees angle and coating the polished surface with a total reflection film. This then allowed the beam to be reflected at a 90 degrees angle creating a side-view probe. For the ball lens probe, the beam can be 90 degree reflected by a 45 degree polished face on the ball lens. The fiber lens tip together with a tubing system and a connected linearly scanning or 360 degrees rotated motor could be built as an endoscope or a needle probe using in the biomedical optical imaging system for *in situ* and *in vivo* minimally invasive diagnostic and/or guided surgery and treatment applications.

As a sample, a needle probe designed for the OCT imaging in this work is shown in Fig. 5 (a). The lens and the uncoated portion of the SMF are protected in a transparent inner catheter (OD 0.49 mm) shown in Fig. 5 (b, c). The buffered portion of the fiber is attached to an outer flexible catheter after the syringe (OD 1.4 mm), which is fastened onto a modified syringe piston, while the transparent inner catheter is inserted into a 21 G (OD 0.81 mm) echogenic spinal needle (VWR, Mississauga, ON, Canada). After insertion into the tissue, the needle can be drawn back while the optical probe stays inside of the tissue as shown in Fig. 5 (b). The probe is then scanned axially inside the tissue driven by a linear scanner, such that a two dimensional OCT image is formed. If a fiber GRIN lens is used, the size of the inner catheter could be as small as 0.4 mm because the diameter of the GRIN lens is smaller than the fiber ball lens.

Figure 5. OCT side-view needle probe showing the tubing and angle-polished ball lens. (a) needle probe. (b) retracted needle tip with protective tubing. (c) protective tubing and exposing the lens.

III. RESULTS

Figure 6. *In vivo* images acquired by our catheter-based complex SS-OCT. (a) Human nail (4x2mm) E: epidermis; SC: stratum corneum; N: nail; BV: blood vessel. (b) Human finger (5x2mm) SG: sweat gland; SL: subcutis layer. (c) onion and (d) fish head of young *Poecilia Wingei* (4x4mm).

In optical coherence tomography, the formation of an image is based on the detection of the interference of low-coherence light that has been backscattered from the probed tissue. Figure 6 shows *in vivo* image samples of human nail (a), human finger (b), fresh onion (c), and fish head of young *Poecilia Wingei* (d) acquired by our catheter-based complex SS-OCT using the 3x3 Mach-Zehnder interferometer and the forward fiber probes # 6 (working distance, depth of field and spot diameter of 1.2 mm 1.1 mm, and 27 μ m). The fine structures, such as epidermis (E), stratum corneum (SC), nail (N), blood vessel (BV), sweat gland (SG), and subcutis layer (SL) in the human nail and finger images, and cells and brain structures in onion and fish head images can be seen clearly.

Figure 7 shows *ex vivo* complex SS-OCT images of tissue of pig heart atrium and ventricle (a,b) and an opened WHHMMI rabbit arterial plaque tissue wall (c) using the forward-view optical fiber probe, and a health rabbit coronary tissue (d) using the side-view optical fiber probe. Three layers of tunica intima (TI), tunica media (TM), and tunica adventitia (TA) of the rabbit artery are viewed clearly as shown in figure 7 (c) and (d) by using both forward-view and side-view probe. The thinner tunica media caused by growing of the lipid and calcification arterial plaque (AP) manifested as dark area has been observed in figure 7 (c).

Figure 7. *Ex vivo* images (4x2mm) of pig heart atrium (a), pig heart ventricle (b), arterial plaque of rabbit (c), and coronary of rabbit (d) acquired by our catheter-based complex SS-OCT.

IV. CONCLUSION

We demonstrate OCT images of the biomedical turbid tissues, such as human skin, onion, fish, pig heart and rabbit arterial plaque using different fiber probes with our complex SS-OCT system. These images offer the possibility to investigate micro-morphologies located on and under the skin or in the arterial tissue wall. The results show that catheter based swept source OCT is an effective imaging modality for real-time diagnosis with high potential for *in vivo* applications.

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